Brain and Spinal Cord Lesions with Long-Term Total Artificial Heart Pumping

Summary. Animals surviving for extended periods with a total artificial heart (TAH) device sometimes experience central nervous system (CNS) complications. These are caused by the hypoperfusion of the CNS for various reasons; by microthromboembolization, which is manifested either by the emboli from a primary thrombotic formation or by calcified emboli; or by central nervous hemorrhages, owing to various causes. The central nervous system can be threatened by hypoperfusion, which may be caused particularly by a mechanical obstruction in the input or output tract of the pump, or by inadequate pumping. Clinically, peripheral spinal paralysis with a histological picture of tigrolysis of the ganglionic cells in the brain and spinal cord and encephalomalacia are frequent findings in these cases. Prevention in these cases can partially depend on proper TAH construction and adequate control and driving. Thromboembolic complications affecting the central nervous system can cause immediate termination of an experiment, if the thromboemboli affect the brain-stem centers. If other parts of the brain are impaired, then for some time this situation can be compatible with life; the animal is mostly hemiplegic before it expires after a few days. From the point of pathogenesis we can differentiate the thrombi caused directly by noncompatible thrombogenic material from those caused by incompatible pump construction resulting in "dead areas" where the bloodstream stagnates and thrombi are formed, or from septic thrombi caused by infection in the animal. On the other hand, the thrombus may be calcified (so-called secondary dystrophic calcification) or the driving diaphragm may be affected by "primary calcification." The prevention of simple thromboembolism may be achieved by adequate TAH construction, by the use of nonthrombogenic material, and by avoiding infection, whereas the prevention of primary calcification may be attained by a special anticalcification treatment. Hemorrhagic lesions affecting the CNS are caused by inadequate anticoagulation and antiaggregation therapy, or by idiopathic endogenous disturbances of coagulation based on septic states or hepatic disturbances caused mostly by an increase in central venous pressure. A solution to the prevention of all possible causes of central nervous disturbance in TAH patients is necessary before its use becomes a clinical reality.

Key words: Total artificial heart — Brain and spinal cord lesions — Hypoperfusion — Thromboembolism — Calcified emboli

Introduction

The artificial heart is a device urgently needed to solve the problem of final heart failure [1–3]. The systems used currently are pneumatic or electromechanical, and they allow only limited comfort for the patient. Therefore, they have been used for short-term application as so-called bridge systems designed for the period preceding heart transplantation. Artificial heart or mechanical heart support systems should be available for these situations. If they are antithrombogenic owing to their construction and mechanical properties, then the patient's central nervous system (CNS) is not so threatened by thromboembolic complications, unless there is infection, which can be the cause of septic thrombi. Even though the Czech artificial heart, TNS-BRNO, is optimal in this respect, in experiments lasting for months, microembolization affecting the CNS, either by primary thrombi or by thromboemboli from the calcified diaphragm, sometimes threatened the duration of survival [4–8]. This danger can be limited by optimal construction of the pump, by a proper antithrombotic treatment, by the prevention of infection, and finally, by affecting the calcification mechanisms biologically or by suitable processing of the diaphragm material to prevent calcifying nucleation. Optimal technology in the production of artificial hearts should entail the complete elimination of potential air embolism into the central nervous system. Therefore, the aim of further research ought to be to design an absolutely defect-free artificial heart which would eliminate any damage to the central nervous system during permanent long-lasting application, owing either to cerebral embolism of any origin, or to CNS hypoperfusion caused by limitations on the pumping capability of the artificial heart.

Materials and Methods

The materials and methods concerning surgery on calves and postoperative care used both in 66 long-term and in short-lasting experiments were published elsewhere [4–6,9–10].
In 62 experiments, a total artificial heart (TAH) TNS-BRNO (model II, III, VII, or VIII) was implanted; in 4 experiments, the ROSTOCK TAH was used [6]. In the short-duration experiments, a TAH TNS-BRNO II or VII was implanted.

The methods for evaluating calcification of the driving diaphragm and the procedure for possible prevention were described elsewhere [4-6].

To assess possible central nervous complications, at the termination of each experiment, a careful autopsy of the central nervous system (brain and spinal cord) was performed and any macroscopic lesions were evaluated. Very important was the evaluation of microscopic sections from all parts of the brain: cortex cerebri, occipital lobe, frontal lobe, parietal lobe, diencephalon, temporal lobe, amygdala region, hippocampus, mesencephalon, brain stem, cerebellum, pons, and medulla oblongata. Several further sections taken from the upper, middle, and lower spinal cord were evaluated. Histological staining methods were: hematoxylin-eosin, methylene blue, von Kossa, Bielschowsky, van Gieson, and Masson’s trichrome. The pathological macro- and microscopic findings in the central nervous system were compared to the clinical symptoms which accompanied death.

Results

In 56 out of 66 animals, the termination of the experiments involved CNS damage from various causes. Tables 1-4 show the four main groups of causes of death where the deleterious effect on the central nervous system was either decisive (the main cause of death) or was at least a serious, accompanying complication. For example, right circulatory insufficiency killed the experimental subject owing to a serious respiratory complication; however, in various parts of brain, serious pathological changes were found. In two calves, observed signs of brain edema, acidotic coloration of the brain tissue, the formation of pseudocysts, dilatation of perivascular spaces in the pons, and dispersed hemorrhages in the thalamus (calves no. 134, “Pluto,” which survived 170 days; and no. 121, “Artur,” which survived 293 days). Table 5 summarizes the CNS lesions observed.

On the other hand, hypoperfusion, due to serious dislocation of the device and thrombi, located in the output tracts, led to definite clinical signs of CNS impairment; e.g., cramps immediately before death (calf no. 122, “Richard,” which survived 166 days of pumping). A similar situation was encountered with the formation of pannus, which markedly decreased the output and caused serious brain damage. Sometimes this situation was enhanced by the dislocation of the pump (calf no. 144, “Arvid,” which survived 190 days) (Fig. 1). In this case, edema with the degeneration of ganglionic cells, red encephalomalacia, and occasional tigrolysis in all parts of the brain were typical of the findings in such a state of hypoperfusion.

Pannus in the left inflow tract with an extreme blockade of the venae pulmonales with accompanying bronchopneumonia was another main cause of inadequate blood supply into the brain (calf no. 116, “Alarich,” which survived 104 days).

Technical failure due to disconnection of the quick connector from the left inflow tract caused massive blood effusion into the space between the pump and the pseudopericardium. Brain death due to multiple foci of local cerebral dystrophy was evident (calf no. 59, “Omar,” which survived 173 days [10]).

Another cause of cerebral death was massive cerebral thromboembolism owing to the formation of septic thrombi as a sequel of massive infection. Polynuclear cells and occasionally small glial knots were observed (calf no. 136, “Nero,” which survived 142 days; calf no. 133, “Hugo,” which survived 110 days; and 16 other cases (Fig. 2).

Successive multiple thromboemboli of calcified material which had broken away from calcified driving diaphragms and migrated into the brain, and marked tigrolysis of cells with encephalomalacia and extensive brain edema, were the causes of death in calf no. 125, “Prokop” (survival 270 days) and no. 123, “Norman” (survival 231 days). However special anticalcification treatment substantially limited the lethal microembolization in the brain and spinal cord by calcified particles in a number of calves

Fig. 1. Calf no. 144, “Arvid.” Survived 190 days of pumping. Cause of death: right circulatory insufficiency. Hippocampus, focus of the red encephalomalacia with the calcified septic microthromboembolus. Magnification 384x; von Kossa stain